REMARKS

The Office Action mailed June 7, 2006 has been carefully considered and the following response prepared. Claims 1-36 are pending in the application. Claims 8, 13-22, 29 and 33-36 are withdrawn from consideration. Claims 1, 7, 8, 9 and 10 have been amended as discussed below. New claims 37 and 38 have been added. Support for new claims 37 and 38 can be found in the specification at page 4, lines 30-35. No new matter has been added.

At page 2 of the Office Action, the Examiner required Applicants to affirm the election of the species of A as GlyPheLeuGly and R^1 and R^2 as H. Applicants affirm the election of species with traverse. Applicants also note that this election is an election of species and other species of A and R^1 and R^2 will be examiner if the elected species is found allowable. Thus, claim 8 should not be withdrawn from consideration as drawn to a non-elected invention as it was placed within Group IV, the elected group of claims. Claims 1-12 are drawn to methods of synthesizing peptides a or a peptide derivative comprising at least two enantiopure amino acids and at least one glycine molecule wherein the peptide has the general formula $R^1R^2NCH_2$-C(=O)-HN-A-COOH (Formula I). The exact amino acid structure of the peptide is not important as long as A, a peptide chain, comprises at least two enantiopure amino acids. Since it is the method of preparing peptides or peptide derivatives that is claimed, not the peptides themselves, it is not reasonable to ask the Applicants to elect a species of peptide made by the process. The restriction/election requirement for this application has in effect turned claim 1 into a process for making only one peptide. As can be plainly seen, claim 1 is useful for preparing peptides of any length and amino acid composition that comprise at least two enantiopure amino acids and one glycine. In order to examine the claimed method, it is not necessary to search any particular peptide or peptide derivative and, therefore, it would not be a burden for the Examiner to

examine the entire scope of claim 1. Withdrawal of the election of species is respectfully requested.

At pages 2-3 of the Office Action, the Applicants were advised that the application is not in compliance with 37 CFR 1.821-1.825. Applicants submit herewith a paper copy of the Sequence Listing, a computer disk containing the Sequence Listing in computer readable form and a Statement to Support Filing and Submission under 37 CFR 1.821-1.825 and 1.52(e)(4). The specification has been amended to insert sequence identifiers. Withdrawal of this objection to the application is respectfully requested.

At page 4 of the Office Action, the Examiner objected to the specification because of informalities. Specifically, the Examiner indicated that the chemical formula on page 12, lines 23-25 has the carbonyl O attached at the incorrect carbon atom. Also, the specification does not contain sequence identifiers in the text where peptide sequences are disclosed.

The chemical formula on page 12, lines 23-25 has been amended to show the carbonyl O attached at the correct carbon atom. Additionally, the specification has been amended to insert sequence identifiers where peptide sequences are disclosed. Withdrawal of these objections to the specification is respectfully requested.

At page 4 of the Office Action, the Examiner objected to claims 1, 7, 9 and 10. Claims 1, 7, 9 and 10 were objected to because they recite "denotes" which the Examiner could indicated could be more clearly stated as "is". Claims 1, 7, 9 and 10 have been amended to delete "denotes" and insert "is" as suggested by the Examiner.

The Examiner also objected to claim 9 because it recites "a fragment C" which the Examiner indicated could be more clearly expressed by using another identifier as C is generally

reserved for use in identifying carbon. Also, the Examiner objected to claim 9 because it does not further limit claim 1, and suggested that claim 9 be amended to state that the method of claim 1 further comprises the recited step of claim 9. Claim 9 has been amended to state that the method of claim 1 further comprises the recited step of claim 9. Applicants respectfully submit that "fragment C" is not confusing. Fragment C is defined in claim 9 as an amino acid or a peptide chain optionally bearing protective and/or activating groups and would not be mistaken for carbon.

Withdrawal of the objections to the claims is respectfully requested.

At page 5 of the Office Action, the Examiner rejected claims 1-7, 9-12, 23-28 and 30-32 under 35 USC 101 because the Examiner asserts the claimed invention is not supported by either a specific and substantial asserted utility, or a well established utility. The basis for the rejection is that the peptides prepared by the claimed method have no specific utility, more particularly, the elected species is asserted to have no specific utility because Smales et al. in which it is disclosed only states that there are possibilities for peptides as components of drug delivery systems.

Applicants traverse this rejection. Claims 1-7, 9-12, 23-28 and 30-32 are directed to methods of preparing a peptide or a peptide derivative comprising at least two enantiopure amino acids and at least one glycine molecule. The peptides produced by the claimed methods have specific and well-established utility. As disclosed in the specification page 1, the peptides produced by the methods of the invention can be used, for example, as medicinal products, as intermediates for producing peptides and as a spacer arm in pharmaceutical compositions intended to take biologically active principles specifically to certain cells of the body. The uses for the peptides produced by the claimed methods are not limited to the specific uses recited in

the specification. Peptides are useful for a number of purposes, such as, including antigens for production of antibodies, linkers (or spacer arms) to join two proteins or peptides and for linking proteins to detectable labels or other compounds. Applicants submit herewith U.S. Patent 5,837,218 (attached as Exhibit A) in which a peptide linker is used to link a peptide and a detectable label. Column 7, lines 45-50 indicate that the linkers can be a peptide of 1-5 amino acid residues and that preferred linking groups include -Gly-Asp-Gly-. Additionally, the peptides produced by the claimed methods can be joined to make proteins such as enzymes and antibodies. The peptides produced by the methods of the invention have specific and well-established utility.

It should be kept in mind that the claimed invention under examination is a method of producing peptides, not the peptides themselves. The claimed methods are useful for producing peptides of any length that are comprised of at least two enantiopure amino acids and at least one glycine molecule. Peptides have specific and well-established utilities. The methods of claims 1-7, 9-12, 23-28 and 30-32 are in compliance with section 101 and withdrawal of this rejection is respectfully requested

At page 7 of the Office Action, the Examiner rejected claims 1-7, 9-12, 23-28 and 30-32 under 35 USC 112, second paragraph. The Examiner stated that claim 1 is indefinite because it recites "Y is chosen from H and cations," and it is unclear whether Y is a cation before binding to carboxylic acid or whether it is a cation that forms a salt of the carboxylic acid. Additionally, the Examiner indicated that "HN-A-COOH" and HN-A-COOY for formulas (I) and (II) in claim 1 wherein a "denotes a peptide chain", and "HN-B" in formula (VI) wherein B "denotes an amino acid or a peptide" in claim 9 are unclear.

Applicants traverse this rejection. Applicants respectfully submit that claims 1 and 9 are not indefinite. It is clear from the specification that A is a peptide chain and that HN- and -COOH and -COOY represent the terminal amino and carboxyl groups, respectively, on the peptide chain. Similarly, it is clear from the specification that HN- in formula (VI) represents the amino group of an amino acid or the terminal amino group of a peptide. Claim 9 has been amended to state that the method of claim 1 further comprises the step recited in claim 9. In view of the amendment to claim 9, it is apparent that the formula variables relate to formula (VI).

Withdrawal of this section 112, second paragraph rejection is respectfully requested.

At page 7 of the Office Action, claims 1-7, 9, 10, 12, 23-28 and 30-32 were rejected under 35 U.S.C. 103(a) as being unpatentable over Smales in view of Marinzi et al., *Bioorg. Med. Chem*, Vol. 9, pages 2323-2328 (2001), Saha et al, *Tetrahedron Letters*, Vol. 36, No. 21, pages 3635-3638 (1995) and Mimura U.S. Patent No. 6,197,998.

Applicants traverse this rejection. Smales et al. discloses the peptide Gly-Phe-Leu-Gly and its synthesis using a method that is different than the claimed methods, as noted by the Examiner. Marinzi et al. discloses synthesis of Nα-substituted Gly-peptide using bromoacetylated peptides that are tethered at the carboxy terminus to a solid support.

Saha et al. discloses synthesis of N-linked-glycopeptoids. In Scheme 2, N-substituted glycine building blocks were prepared from t-butyl bromoacetate to which was added a primary amine to form leucine, phenylalanine and alanine analogues. Dipeptoid units were formed by coupling the glycine building blocks with an N-acetylglucosamine substituted amine. The dipeptoid unit was further elongated by treatment with acid.

Mimura discloses synthesis of glycyl-tyrosine using chloroacetyltyrosine and aqueous ammonia (Example 2, column 5).

In the claimed methods, peptides comprising at least two enantiopure amino acids and at least one glycine molecule are prepared by reacting a compound of general formula XCH_2-C(=O)-HN-A-COOY (II), in which X is a group which can be substituted by nucleophilic substitution, chosen from Cl and Br, and Y is chosen from H and cations, A has the same meaning as in formula (I); with a compound of general formula HNR^1R^2 (III) in which R^1 and R^2 have the same meaning as in formula (I) (i.e., A is a peptide chain comprising at least two enantiopure amino acids; and R^1 and R^2 are chosen, independently, from H or alkyl, alkenyl and aryl which are optionally functionalized, a peptide and a nucleic acid, or R^1 and R^2 together form a cycloalkyl or cycloheteroalkyl substituent).

The methods of claims 1-7, 9, 10, 12, 23-28 and 30-32 are not obvious in view of the combined teachings of Smales et al., Marinzi et al. Saha et al. and Mimura. Smales et al. is not relevant to the claimed methods. Smales et al. does not disclose any of the steps of the claimed methods. The methods in Saha et al. produce a peptoid based on glycine that has no chiral centers, rather than a peptide as produced by the claimed methods. The method disclosed in Marinzi et al. uses peptides tethered to a solid support, whereas the reactants in the claimed methods are free in solution. There is no disclosure or suggestion in Mimura of preparing peptides, and there is no reasonable expectation that the method disclosed therein could be used to synthesize longer peptides. Moreover, there is no disclosure or suggestion in the combined teachings of the references of preparing peptides comprised of at least two enantiopure amino acids and glycine. The combined teachings of the cited references neither disclose nor suggest

the methods of claims 1-7, 9, 10, 12, 23-28 and 30-32. Withdrawal of this section 103 rejection is respectfully requested.

At page 11 of the Office Action, claims 1-7, 9-12, 23-28 and 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Smales in view of Marinzi, Saha and Mimura, as applied to claims 1-7, 9, 10, 12, 23-28 and 30-32, *supra*, and in further view of Anteunis U.S. Patent No. 4,725,645.

Applicants traverse this rejection. Smales in view of Marinzi, Saha and Mimura were discussed above. Anteunis et al. is concerned with the preparation of peptides that uses a coupling reaction wherein the amino acid reactants are activated with trialkylsilanes that facilitate the formation of peptide bonds.

The methods of claims 9 and 11 refer to activating agents. The amendments to claim 9 make it clear that the step recited in claim 9 for preparing the compound of formula (II) is a separate step and not performed at the same time or as part of the step of the method of claim 1. The compound of formula (II) is a reactant in the method of claim 1. Anteunis et al. is not relevant to the method of claim 1. Anteunis et al. therefore adds nothing to the teachings of Smales et al., Marinzi et al., Saha et al. and Mimura that would render obvious the methods of claims 1-7, 9, 10, 12, 23-28 and 30-32. There is no disclosure or suggestion in the combined teachings of the references of preparing peptides comprised of at least two enantiopure amino acids and glycine. The combined teachings of the cited references neither disclose nor suggest the methods of claims 1-7, 9, 10, 12, 23-28 and 30-32. Withdrawal of this section 103 rejection is respectfully requested.

In view of the above amendment, applicant believes the pending application is in condition for allowance. Reconsideration of the application is respectfully requested and an early Notice of Allowance is earnestly solicited.

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Respectfully submitted,

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